

The relationship between nutritional parameters and pregnancy outcomes in abortus imminens

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ABSTRACT

Aims: Abortus imminens (AI) is defined as vaginal bleeding and/or pelvic pain before the 20th week of pregnancy. It affects approximately 20% of pregnancies. The HALP score, which integrates hemoglobin, albumin, lymphocyte, and platelet levels, is a marker of inflammation and nutritional status. This study investigates the association between the HALP score and AI and its potential role in predicting pregnancy outcomes.

Methods: This retrospective study was conducted at Ankara Etlik City Hospital between September 2022 and March 2024. A total of 254 patients with AI and 260 controls were included. Data on maternal demographics and laboratory parameters, including hemoglobin, albumin, lymphocyte, and platelet levels, were collected. Statistical analyses were performed using SPSS 22.0, with significance set at $p < 0.05$.

Results: The HALP score was significantly higher in the AI group than in controls ($p = 0.002$). However, no significant difference in HALP scores was observed between patients who experienced pregnancy loss and those who continued their pregnancies ($p = 0.350$). Preterm birth, newborn intensive care unit admission, and respiratory distress were more frequent in AI cases.

Conclusion: The HALP score is a practical and cost-effective tool for diagnosing AI. Further studies are needed to explore its clinical utility.

Keywords: Abortus imminens, HALP score, nutrition, pregnancy outcomes

INTRODUCTION

Vaginal bleeding and/or pelvic pain that occur prior to the twentieth week of pregnancy are known as abortus imminens (AI).^{1,2} It occurs more frequently in the first trimester of pregnancy and complicates about one fifth of all pregnancies.³ Although not every patient followed up for AI experiences miscarriage, these patients may experience adverse obstetric outcomes such as premature birth, fetal death in utero, bleeding before birth and low birth weight in the later weeks of pregnancy.⁴ The etiology includes maternal diseases (such as diabetes mellitus, kidney and thyroid diseases), malnutrition and underweight, maternal and fetal infections, cervical insufficiency, fetal anomalies and previous surgical interventions (such as chorionic villus sampling). A history of AI in a previous pregnancy, a low socio-economic class, older maternal age, smoking and alcohol consumption also increase the risk of AI.⁵⁻⁸

There is no optimal parameter that predicts the diagnosis and course of pregnancy in AI patients. For this goal, previous

research has looked at serum amyloid A, serum thiol/disulfide, serum leptin levels, and a variety of inflammatory markers, including interleukin-2 (IL-2), IL-4, interferon- γ , and IL-13. However, these parameters were not examined as part of routine laboratory tests.^{3,7,9-11} The HALP score was initially established in 2015 and is based on factors like hemoglobin, albumin, lymphocytes, and platelets.¹² The presence of nutrition-related parameters such as hemoglobin and albumin and inflammation-related parameters such as platelets and lymphocytes make this score an important indicator of both inflammation and nutrition.¹²⁻¹⁴ The HALP score has emerged as one of the most significant predictors of death and morbidity in recent years, particularly in research involving cancer patients.¹⁵⁻¹⁸ Furthermore, the HALP score is a cheap assessment that is simple to compute using standard laboratory measurements.

Predicting the pregnancy's trajectory and the likelihood of an abortion in patients with AI is crucial for patient education,

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management, and postpartum care. We aimed to assess the relationship between the HALP score, an immuno-nutritional score, and AI and ascertain whether it can aid in clinical treatment procedures, given that infections, malnutrition, and underweight are some of the factors that lead to AI.

METHODS

Between September 2022 and March 2024, this study was carried out retrospectively in the Perinatology Department of Ankara Etlik City Hospital, a tertiary facility to which patients were referred from various centers. The sample was divided into 2 groups: 254 patients with AI and 260 control patients. Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee authorised the study protocol (Date: 25.12.2024, Decision No: AESH-BADEK-2024-1142). The Declaration of Helsinki's guidelines were followed in the conduct of this study.

AI occurs when there is vaginal bleeding, a mean gestational sac diameter of more than 25 mm, a crown-rump length (CRL) of more than 7 mm, and an ultrasound showing a fetal heartbeat.¹⁹ Patients with an AI diagnosis between weeks 8 and 12 of pregnancy were included in the study. Age and weeks of diagnosis were matched to create a control group. The starting day of the last menstrual cycle was used to calculate the gestational age of the patients who were part of the study. In patients whose last menstruation was unknown, the week determination was calculated using the CRL at ultrasound examination during hospitalization. Exclusion criteria included chronic maternal illness, medication use, smoking, alcohol consumption, presence of congenital anomalies, multiple pregnancies, patients whose information could not be reached or who had given birth at an external center. During the study period, 342 patients with a diagnosis of AI were interned in our clinic. Thirty-three patients suffered from long-term maternal conditions: twelve had hypothyroidism, eleven had type 2 diabetes, two had type 1 diabetes, two had chronic hypertension, two had mitral and tricuspid regurgitation, one had end-stage renal disease, one had systemic lupus erythematosus, one had major depression, and one had ankylosing spondylitis. Furthermore, 6 patients had multiple pregnancies (5 twin pregnancies and 1 triplet pregnancy), while 8 patients smoked. 41 patients were excluded because they were followed up at an external center. As a result, 254 patients remained in the research after 88 patients who met the exclusion criteria were removed (Figure 1). Our hospital's data network was used to evaluate the patients' medical records in the past; demographic information was noted, including height, weight, mother age, and parity. Maternal venous blood was used to test hemoglobin, monocyte, white blood cell (WBC) count, lymphocyte, neutrophil, monocyte, platelet, and albumin levels at the time of diagnosis. $[\text{Hemoglobin (g/L)} \times \text{albumin (g/L)} \times \text{lymphocytes (/L)}] / \text{platelets (/L)}$ was the formula used to create the HALP score.^{12,13}

Obstetric complications such as spontaneous abortion and missed abortion that occurred during pregnancy follow-up of the patients were recorded and followed up accordingly. Spontaneous abortion was defined as expulsion of fetal

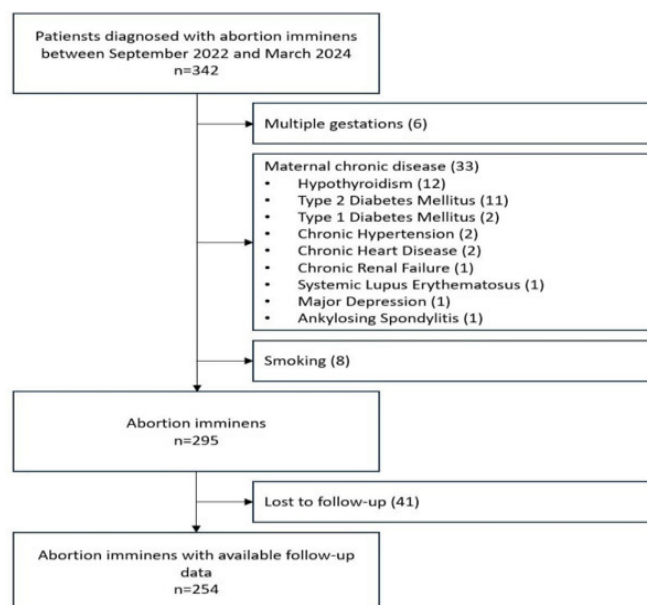


Figure 1. Flow chart

tissue weighing less than 500 grams or before the 20th week of gestation.²⁰ Missed abortion is defined as a pregnancy remaining in the uterus after the death of the embryo or fetus.²¹ To reduce the risk of progesterone insufficiency, patients with a diagnosis of AI who were admitted to the hospital were given 200 mg of natural micronized progesterone orally or intravaginally twice a day in our clinic. Additionally, patients with a maternal blood group that is Rhesus negative (Rh-negative) were given anti-D immunoglobulin (anti-D). The type of delivery, birth weight, sex, APGAR 1/APGAR 5 score and all neonatal morbidities were recorded.

Statistical Analysis

IBM Corporation SPSS version 22.0 (IBM Corporation, Armonk, NY, USA) was used to conduct the statistical analysis. The conformance to the normal distribution was examined using the Kolmogorov-Smirnov test. For continuous variables having a normal distribution, descriptive statistics are displayed as "mean±standard deviation"; for those without, they are displayed as "median (interquartile range)". Fisher's-Exact test or the Chi-squared test were used to compare categorical variables. The Independent Sample T-test and the Mann-Whitney U test were used to compare continuous variables that were and were not regularly distributed. The best cutoff values were determined by calculating and comparing the areas under the curve (AUC) using a receiver operator characteristic (ROC) curve. For all tests, a p-value of less than 0.05 was considered statistically significant.

RESULTS

There were 260 controls and 254 patients with AI in this study. The demographic information for the two groups is displayed in Table 1. Both groups had comparable maternal ages, gravidities, parities, and nulliparities ($p=0.574$, $p=0.418$, $p=0.379$, and $p=0.296$, respectively). AI patients had a considerably lower body-mass index (BMI) than control patients ($p<0.001$). The median week of diagnosis of patients in the abortus imminens group was 9 weeks.

Table 1. Descriptive and comparative analysis of demographic data between abortus imminens and control groups

Parameter	Abortus imminens n=254 (49.4%)	Control n=260 (50.6%)	P
Age (y)	28.9±5.6	28.7±5.4	0.574 ^a
Body-mass index (kg/m ²)	28±5	29.6±5	<0.001 ^a
Gravida	2 (2)	2 (2)	0.418 ^b
Parity	1 (2)	1 (2)	0.379 ^b
Nulliparous	129 (50.8%)	144 (55.4%)	0.296 ^c

Values were given as mean±standard deviation, median (interquartile range), number (%). p<0.05 was considered statistically significant. a: Student t-test, b: Mann-Whitney U, c: Chi-square

The laboratory results for the individuals who were part of the trial throughout the first trimester are displayed in **Table 2**. The HALP score was substantially higher in the abortion imminens group (p=0.002), standing at 37.9 (22.7) compared to 34.9 (14.5) in the control group. The AI group's hemoglobin levels were considerably greater than those of the control group (p=0.002). Patients with AI had reduced platelet and lymphocyte counts (p<0.001, p=0.007). WBC, neutrophil, monocyte, and albumin counts, among other laboratory indicators, were comparable in both groups (p=0.363, p=0.414, p=0.937, and p=0.106, respectively).

Table 2. Comparison of the patients groups' first trimester laboratory and HALP scores

	Abortus imminens n=254 (49.4%)	Control n=260 (50.6%)	P
HALP score	37.9 (22.7)	34.9 (14.5)	0.002 ^a
Hemoglobin (g/dl)	12.7 (1.8)	12.4 (1.8)	0.002 ^a
WBC count (10 ⁹ /L)	9.54 (3.13)	9.05 (3.11)	0.363 ^a
Lymphocyte count (10 ⁹ /L)	1.93 (0.75)	2.17 (1.07)	<0.001 ^a
Neutrophil count (10 ⁹ /L)	6.51 (2.89)	6.36 (2.74)	0.414 ^a
Monocyte count (10 ⁹ /L)	0.59 (0.22)	0.59 (0.22)	0.937 ^a
Platelet count (10 ⁹ /L)	250 (77)	271 (69)	0.007 ^a
Albumin (g/L)	37.3 (3.4)	37.8 (8.8)	0.106 ^a

HALP score: The hemoglobin, albumin, lymphocyte, and platelet score; WBC: White blood cell, a: Mann-Whitney U test

The neonatal outcomes of the study participants are displayed in **Table 3**. 193 (76%) of the 254 patients with AI who were enrolled in the trial did not have an abortion. There were 61 patients (24%) who underwent an abortion. Of these, 41 (16.1%) were assessed as spontaneous abortions and 20 (7.9%) as missed abortions (**Figure 2**). The HALP score was 38.4 (23.2) in patients diagnosed with AI and subsequent abortion and 36.9 (25.1) in the group without abortion, and there was no significant difference between the two groups (p=0.350). In the AI patients, the results of the newborns were examined. Delivery occurred at earlier weeks and birth weight was lower compared to the control group (p<0.001 and p<0.001, respectively). In comparison to the control group, the AI group experienced significantly more preterm births, newborn intensive care unit (NICU) hospitalizations, respiratory distress syndrome (RDS), and continuous positive airway pressure (CPAP) (p=0.001, p<0.001, p<0.001, and p=0.003, respectively). Pregnancy termination way, gender, APGAR 1st min, APGAR 5th min, fetal distress, neonatal hypoglycemia, transient tachypnea

of the newborn (TTN), mechanical ventilation, neonatal phototherapy, intraventricular hemorrhage, neonatal sepsis, neonatal seizures and necrotizing enterocolitis numbers were similar in both groups (p= 0.429, p= 0.606, p=0.909, p=0.544, p=0.322, p=0.492, p=0.168, p=0.055, p=0.662, p=0.426, p=0.426, p=0.426, respectively).

Table 3. Comparison of findings regarding newborn characteristics and labor

Parameter	Abortus imminens n=193 (42.6%)	Control n=260 (57.4%)	P
Gestational weeks at delivery	38 (2)	39 (2)	<0.001 ^a
Pregnancy termination way			0.429 ^b
Cesarean section	117 (60.6%)	148 (56.9%)	
Normal spontaneous vaginal birth	76 (39.4%)	112 (43.1%)	
Gender			0.606 ^b
Female	94 (48.7%)	133 (51.2%)	
Male	99 (51.3%)	127 (48.8%)	
Fetal weight (gr)	2981 ± 612	3186 ± 506	<0.001 ^c
1 st min. APGAR	9 (1)	9 (1)	0.909 ^a
5 th min. APGAR	10 (1)	10 (0)	0.544 ^a
Fetal distress	20 (10.4%)	20 (7.7%)	0.322 ^b
Preterm birth	44 (22.8%)	30 (11.5%)	0.001 ^b
Admission to neonatal intensive care unit	40 (20.7%)	23 (8.8%)	<0.001 ^b
Neonatal hypoglycemia	16 (6.2%)	9 (4.7%)	0.492 ^b
Transient tachypnea of the newborn	12 (6.2%)	9 (3.5%)	0.168 ^b
Respiratory distress syndrome	20 (10.4%)	6 (2.3%)	<0.001 ^b
Continues positive airway pressure	26 (13.5%)	14 (5.4%)	0.003 ^b
Mechanical ventilation	10 (5.2%)	5 (1.9%)	0.055 ^b
Phototherapy for neonates	13 (6.8%)	15 (5.8%)	0.662 ^b
Intraventricular hemorrhage	1 (0.5%)	0 (0%)	0.426 ^d
Neonatal sepsis	1 (0.5%)	0 (0%)	0.426 ^d
Neonatal seizures	1 (0.5%)	0 (0%)	0.426 ^d
Necrotizing enterocolitis	1 (0.5%)	0 (0%)	0.426 ^d

^a: Mann-Whitney U test, ^b: Chi-square, ^c: Student t-test, ^d: Fisher's exact test

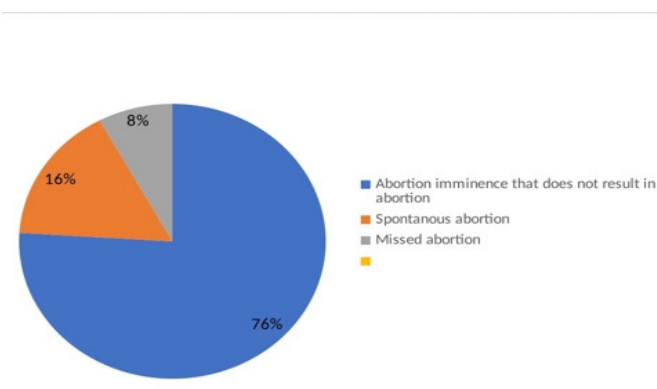
**Figure 2.** Outcomes of patients with abortus imminens

Table 4. Evaluation of HALP score in abortus imminens and control groups by ROC analysis

	LR+	Cut-off*	Sensitivity	Specificity	AUC	%95 CI	p
HALP score	1.24	>3.61	54.8%	55.9%	0.582	0.53–0.63	0.002

*Cut-off values were found according to Youden index. HALP score: The hemoglobin, albumin, lymphocyte, and platelet score, ROC: Receiver operator characteristic, LR+: Positive likelihood ratio, AUC: Area under the curve, CI: Confidence interval

The ROC analysis of the HALP score is displayed in **Table 4**. AI is diagnosed with a sensitivity of 54.8% and a specificity of 55.9% when the HALP score is greater than the cut-off value of 36.1 (AUC: 0.582, $p=0.002$). In **Figure 3**, the HALP score's ROC curve is displayed.

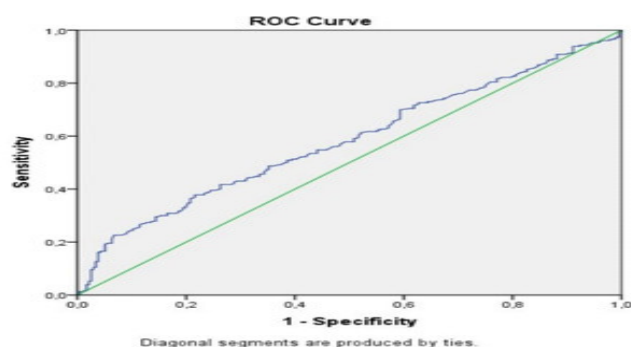


Figure 3. The ROC curve of HALP score
HALP score: The hemoglobin, albumin, lymphocyte, and platelet score, ROC: Receiver operator characteristic

DISCUSSION

This study investigated the relationship between AI diagnosis and pregnancy outcome and the HALP score. It was discovered that the AI group's HALP score was noticeably greater than the control group's. An AI is diagnosed with a sensitivity of 54.8% and a specificity of 55.9% when the HALP score is more than 36.1 (AUC: 0.582, $p=0.002$). In this study, the AI group had a lower gestational age and birth weight, but a greater preterm birth rate, NICU hospitalization, RDS, and CPAP. In the AI group, the HALP score no correlation with abortion rates or adverse perinatal outcomes. Additionally, this is the only study that we are aware of that looks into the relationship between AI patients and the HALP score.

Although the etiology of AI is multifactorial, one of the most emphasized causes is inflammation. Soysal et al.²⁰ have investigated the connection between AI and the inflammation-related systemic immune inflammatory index, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and monocyte-to-lymphocyte ratio. During follow-up, it was discovered that AI patients had a considerably higher systemic immune inflammation index, which was linked to abortion.²⁰ Antiapolipoprotein A-1, which can be associated with inflammation, was also studied in AI patients by Vecchié et al.²² and was found to be high in AI patients. Fetal development is influenced by the nutritional state of the mother. Negative obstetric outcomes are closely linked to malnutrition, a complicated condition marked by low protein stores, insufficient caloric intake, and a compromised immune system.²³ Hemoglobin and albumin are the parameters most commonly used in the clinic to determine the nutritional status of patients. Low albumin and anemia are associated in the literature with increased mortality and morbidity, especially in cancer patients.^{12,24,25} Platelet count, lymphocyte count, hemoglobin and albumin levels

are all part of the HALP score, a nutritional inflammation index that was initially established in 2015 in patients with stomach cancer.¹² Investigations on the relationship between the HALP score and the severity of the condition in patients with pre-eclampsia revealed that the HALP score increased significantly with pre-eclampsia severity.²⁶ The connection between AI and HALP becomes even more significant when one takes into account the roles that inflammation and diet play in the genesis of AI. The HALP score in our investigation indicated a substantial difference in AI diagnosis.

One common obstetric problem that can be linked to abortions is bleeding during the first trimester of pregnancy. Studies have shown that 14% to 50% of patients with AI who present with vaginal bleeding have had a abortions.^{27,28} In our study, the number of patients who had an abortion was 61 (24%). We also compared the HALP scores between these patients and those whose pregnancies were continued. The HALP score was 38.4 (23.2) in the patients who were diagnosed with AI and subsequently had an abortion, and 36.9 (25.1) in the group who did not have an abortion, with no significant difference between the two groups. This situation may be due to the multifactorial etiology of AI as well as the patient's current intake of oral iron supplements, physiologic vascular changes in pregnancy, dehydration due to malnutrition, or changes in laboratory parameters measured from maternal blood, depending on the severity of the patient's bleeding.

In a study that compiled 14 articles, Saraswat et al.²⁹ assessed perinatal mortality and morbidity in AI patients. They showed that AI patients had lower APGAR ratings, a higher risk of NICU admissions, and a higher rate of preterm birth and low birth weight. Similarly, in their study, Özdemirci et al.³⁰ discovered that AI patients had a higher rate of low birth weight and premature birth. In our study, lower gestational age and birth weight as well as higher preterm birth, NICU admission, RDS and CPAP rates were found in the data of patients interned due to AI. However, no association was found between adverse perinatal outcomes and the HALP score. This situation can be explained by the multifactorial etiology of AI, but shows that more parameters should be evaluated together when predicting pregnancy outcomes.

Limitations

The retrospective design of our study and the limited number of patients make it difficult to evaluate the cause-effect relationship. Although chronic diseases and drug use, which would increase the effects on maternity, were not among the exclusion criteria, we may not have been able to exclude all factors that could affect hemoglobin, platelet, lymphocyte, and albumin levels. In addition, the fact that the data come from a single center limits the generalizability of the results, and the change in these parameters over time could not be taken into account. Prospective studies with a larger number

of patients could more clearly show the impact of the HALP score on assisted reproduction and obstetric outcomes.

CONCLUSION

The affordability and ease of calculation of the HALP score using routine laboratory parameters enhance its potential applicability in clinical practice. As a cost-effective and accessible tool, it may serve as a supplementary marker in evaluating patients with AI. According to our research, while the HALP score demonstrates some diagnostic value in AI, its predictive capacity for adverse pregnancy outcomes remains limited. This highlights the need for a more comprehensive approach in assessing pregnancy prognosis in AI patients.

Although the HALP score was significantly higher in the AI group compared to controls, no significant association was found between HALP levels and pregnancy loss or adverse neonatal outcomes. This suggests that while inflammation and nutritional status play a role in the pathophysiology of AI, the HALP score alone may not be sufficient to predict pregnancy trajectory.

Future research should also explore the interaction between HALP and other emerging biomarkers to develop more accurate predictive models for pregnancy outcomes in AI. Investigating HALP's potential role in different AI subgroups, such as those with recurrent pregnancy loss, autoimmune conditions, or infections, could yield valuable clinical insights. Furthermore, assessing the impact of targeted nutritional or anti-inflammatory interventions on HALP levels and pregnancy outcomes may provide evidence for novel therapeutic approaches.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee authorised the study protocol (Date: 25.12.2024, Decision No: AESH-BADEK-2024-1142).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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